



Agency for Healthcare Research and Quality
Advancing Excellence in Health Care



NATIONAL
GUIDELINE
CLEARINGHOUSE

General

Guideline Title

Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer: U.S. Preventive Services Task Force recommendation statement.

Bibliographic Source(s)

U.S. Preventive Services Task Force. Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2014 Apr 15;160(8):558-64. [26 references]

[PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Routine vitamin supplementation to prevent cancer and cardiovascular disease: recommendations and rationale. *Ann Intern Med.* 2003 Jul 1;139(1):51-5. [42 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations (A, B, C, D, or I) and identifies the levels of certainty regarding net benefit (High, Moderate, and Low). The definitions of these grades can be found at the end of the "Major Recommendations" field.

Summary of Recommendations and Evidence

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of multivitamins for the prevention of cardiovascular disease or cancer. (I statement)

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of single- or paired-nutrient supplements (except β -carotene and vitamin E) for the prevention of cardiovascular disease or cancer. (I statement)

The USPSTF recommends against β -carotene or vitamin E supplements for the prevention of cardiovascular disease or cancer. (D recommendation)

Clinical Considerations

Patient Population Under Consideration

The focus of this recommendation is healthy adults without special nutritional needs. Populations studied were typically aged 50 years or older. This recommendation does not apply to children, women who are pregnant or may become pregnant, or persons who are chronically ill or hospitalized or have a known nutritional deficiency.

Suggestions for Practice Regarding the I Statements

Potential Preventable Burden

Evidence from in vitro and animal research and population-based epidemiologic studies supports the hypothesis that oxidative stress may play a fundamental role in the initiation and progression of cancer and common cardiovascular diseases. If this hypothesis is correct, then some combination of specific supplements, a specific dose, a vulnerable host, and specific timing may be found to be useful.

Potential Harms

Important harms have been shown with β -carotene in persons who smoke tobacco or have an occupational exposure to asbestos. There are several known adverse effects caused by excessive doses of vitamins; for example, moderate doses of vitamin A supplements may reduce bone mineral density, but high doses may be hepatotoxic or teratogenic. Otherwise, the vitamins reviewed by the USPSTF had few known risks. Because many of these vitamins are fat-soluble, the lifetime effect of high doses should be taken into consideration.

The USPSTF did not address doses higher than the tolerable upper intake level, as determined by the U.S. Food and Nutrition Board. Vitamins A and D have known harms at doses exceeding the tolerable upper intake levels, and the potential for harm from other supplements at high doses should be carefully considered.

The U.S. Pharmacopeia has developed reference standards to aid in quality control of dietary supplement production; however, the content and concentration of ingredients in commercially available formulations probably vary considerably. This variability in the composition of dietary supplements makes extrapolating results obtained from controlled clinical trials challenging.

Costs

Although dietary supplements themselves are not particularly costly, the cumulative effect of this class of agent on spending is substantial. In 2010, \$28.1 billion was spent on dietary supplements in the United States.

Current Practice

Surveys conducted by the dietary supplement industry suggest that many physicians and nurses have recommended dietary supplements to their patients for health and wellness.

Additional Approaches to Prevention

Appropriate intake of vitamin and mineral nutrients is essential to overall health. Despite the uncertain benefit of vitamin supplementation, the 2010 Dietary Guidelines for Americans suggest that nutrients come primarily from foods and provide guidance on how to consume a nutrient-rich diet. Adequate nutrition by eating a diet rich in fruits, vegetables, whole grains, fat-free and low-fat dairy products, and seafood has been associated with a reduced risk for cardiovascular disease and cancer.

Specific groups of patients with well-defined conditions may benefit from specific nutrients. For example, women who are planning to or may become pregnant should receive a daily supplement containing folic acid to help prevent neural tube defects. The USPSTF also recommends vitamin D supplements for older persons at risk for falling.

Useful Resources

The USPSTF has a large portfolio of recommendations for prevention of cardiovascular disease and cancer, including recommendations for smoking cessation; screening for lipid disorders, hypertension, diabetes, and cancer; obesity screening and counseling; and aspirin use (available from the [USPSTF Web site](#)).

Definitions:

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer/provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If this service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	<p>The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as:</p> <ul style="list-style-type: none"> • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice • Lack of coherence in the chain of evidence <p>As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.</p>
Low	<p>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:</p> <ul style="list-style-type: none"> • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice • A lack of information on important health outcomes <p>More information may allow an estimation of effects on health outcomes.</p>

Clinical Algorithm(s)

None available

Scope

Disease/Condition(s)

- Cancer
- Cardiovascular disease

Guideline Category

Assessment of Therapeutic Effectiveness

Prevention

Clinical Specialty

Cardiology

Family Practice

Internal Medicine

Nursing

Nutrition

Oncology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

- To summarize the U.S. Preventive Services Task Force (USPSTF) recommendations on vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease (CVD) and cancer
- To update the 2003 USPSTF recommendation on vitamin supplementation to prevent CVD and cancer

Target Population

Healthy adults without special nutritional needs

Note: This U.S. Preventive Services Task Force recommendation statement does not apply to children, women who are pregnant or may become pregnant, or persons who are chronically ill or hospitalized or have a known nutritional deficiency.

Interventions and Practices Considered

Routine vitamin supplementation with:

- Multivitamins
- Single- or paired-nutrient supplements
- β -carotene
- Vitamin E

Major Outcomes Considered

- Key Question 1: What is the efficacy of multivitamin supplement use on health outcomes in the general adult population?
- Key Question 2: What is known about the safety of multivitamin supplement use in the general adult population?
- Key Question 3: What is the efficacy of supplementation with single nutrients or functionally related nutrient pairs on health outcomes in the general adult population?
- Key Question 4: What is known about the safety of single nutrient use in the general adult population?

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by the Kaiser Permanente Research Affiliates Evidence-based Practice Center (EPC), Kaiser Permanente Center for Health Research for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Data Sources and Searches

EPC staff reviewed all included studies from 3 USPSTF reviews published in 2003 and the review conducted by Huang and colleagues. The staff searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Database of Abstracts of Reviews of Effects from January 2005 through January 29, 2013, to identify articles published since the review conducted by Huang and colleagues. The EPC staff also searched the bibliographies of relevant reviews and meta-analyses, as well as the Web sites of government agencies and professional organizations, for any relevant research published outside of peer-reviewed journals. The staff obtained additional references from outside experts.

Study Selection

Two investigators independently reviewed each study's abstract against prespecified inclusion criteria. The EPC staff included fair- and good-quality randomized, controlled trials that assessed the effectiveness or safety of supplements in the primary prevention of cardiovascular disease (CVD), cancer, or all-cause mortality in the general adult population without a history of CVD or cancer. The staff included fair- and good-quality

secondary prevention trials if they hypothesized effects on outcomes included in this review and not present at baseline in the study (for example, a trial of secondary skin cancer prevention that also reported on other cancers). The EPC staff included only studies that were conducted among community-dwelling, nutrient-sufficient adults who had no chronic disease and were performed in countries with a Human Development Index of "very high." The staff also required supplement doses to be lower than the upper tolerable limit set by the U.S. Food and Nutrition Board. They included both fair- and good-quality trials and observational studies, without limitations on study sample size or duration, to assess potential harms in order to increase the likelihood of detecting serious harms that are rare or that develop only after long time periods. Serious harms included paradoxical increases in CVD, cancer, or mortality and events defined as "serious" by study investigators. The EPC staff also considered adverse events in trials that reported less serious harms if they were common (that is, occurred in >5% of persons and were statistically significantly higher among those receiving supplements).

Number of Source Documents

- Key Question 1: 11 articles (3 trials)
- Key Question 2: 6 articles (5 studies)
- Key Question 3: 82 articles (18 trials)
- Key Question 4: 55 articles (23 studies)

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Two reviewers independently assessed the methodological quality of each study using predefined criteria developed by the U.S. Preventive Services Task Force and supplemented with the National Institute for Health and Clinical Excellence methodology checklists for observational studies (see Appendix B Table 2 in the Evidence Synthesis [see the "Availability of Companion Documents" field]).

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was prepared by the Kaiser Permanente Research Affiliates Evidence-based Practice Center (EPC), Kaiser Permanente Center for Health Research for the U.S. Preventive Services Task Force (USPSTF) (see the "Availability of Companion Documents" field).

Data Extraction and Quality Assessment

One investigator abstracted study design information, baseline population characteristics, intervention details, disease incidence, mortality, and harms data from all included studies into a standardized evidence table. A second investigator checked these data for accuracy. Two investigators independently assessed each study's quality as "good," "fair," or "poor" by using predefined quality criteria based on USPSTF methods. The EPC staff excluded all poor quality randomized, controlled trials and observational studies. In general, a good-quality study met all prespecified criteria. A fair-quality study did not meet at least one criterion but also did not have a known limitation that could invalidate its results. A poor-quality study had a fatal flaw or multiple important limitations. The EPC staff supplemented the USPSTF criteria with criteria from the National Institute for Health and Clinical Excellence for the quality assessment of observational studies. The EPC staff resolved any disagreements through discussion.

Data Synthesis and Analysis

The EPC staff qualitatively described and summarized the evidence. They stratified results by supplement and synthesized the results of included studies by examining estimates of effects. The staff conducted meta-analyses to estimate the effect size of supplementation on cardiovascular disease (CVD) incidence, cancer incidence, and all-cause mortality at the longest follow-up time point by using the metan procedure of Stata software, version 11.2 (Stata Corp., College Station, Texas). For all cases, the EPC staff analyzed unadjusted relative risks based on the number of events and nonevents. They used the fixed-effects Mantel–Haenszel method because few trials could be combined and to help avoid bias associated with rare events (1% to 10% of participants in most trials).

Methods Used to Formulate the Recommendations

Balance Sheets
Expert Consensus

Description of Methods Used to Formulate the Recommendations

The U.S. Preventive Services Task Force (USPSTF) systematically reviews the evidence concerning both the benefits and harms of widespread implementation of a preventive service. It then assesses the certainty of the evidence and the magnitude of the benefits and harms. On the basis of this assessment, the USPSTF assigns a letter grade to each preventive service signifying its recommendation about provision of the service (see Table below). An important, but often challenging, step is determining the balance between benefits and harms to estimate "net benefit" (that is, benefits minus harms).

Table 1. U.S. Preventive Services Task Force Recommendation Grid*

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	Insufficient			

*A, B, C, D, and I (*Insufficient*) represent the letter grades of recommendation or statement of insufficient evidence assigned by the USPSTF after assessing certainty and magnitude of net benefit of the service (see the "Rating Scheme for the Strength of the Recommendations" field).

The overarching question that the USPSTF seeks to answer for every preventive service is whether evidence suggests that provision of the service would improve health outcomes if implemented in a general primary care population. For screening topics, this standard could be met by a large randomized, controlled trial (RCT) in a representative asymptomatic population with follow-up of all members of both the group "invited for screening" and the group "not invited for screening."

Direct RCT evidence about screening is often unavailable, so the USPSTF considers indirect evidence. To guide its selection of indirect evidence, the USPSTF constructs a "chain of evidence" within an analytic framework. For each key question, the body of pertinent literature is critically appraised, focusing on the following 6 questions:

1. Do the studies have the appropriate research design to answer the key question(s)?
2. To what extent are the existing studies of high quality? (i.e., what is the internal validity?)
3. To what extent are the results of the studies generalizable to the general U.S. primary care population and situation? (i.e., what is the external validity?)
4. How many studies have been conducted that address the key question(s)? How large are the studies? (i.e., what is the precision of the evidence?)
5. How consistent are the results of the studies?
6. Are there additional factors that assist the USPSTF in drawing conclusions (e.g., presence or absence of dose–response effects, fit within a biologic model)?

The next step in the USPSTF process is to use the evidence from the key questions to assess whether there would be net benefit if the service

were implemented. In 2001, the USPSTF published an article that documented its systematic processes of evidence evaluation and recommendation development. At that time, the USPSTF's overall assessment of evidence was described as good, fair, or poor. The USPSTF realized that this rating seemed to apply only to how well studies were conducted and did not fully capture all of the issues that go into an overall assessment of the evidence about net benefit. To avoid confusion, the USPSTF has changed its terminology. Whereas individual study quality will continue to be characterized as good, fair, or poor, the term certainty will now be used to describe the USPSTF's assessment of the overall body of evidence about net benefit of a preventive service and the likelihood that the assessment is correct. Certainty will be determined by considering all 6 questions listed above; the judgment about certainty will be described as high, moderate, or low.

In making its assessment of certainty about net benefit, the evaluation of the evidence from each key question plays a primary role. It is important to note that the USPSTF makes recommendations for real-world medical practice in the United States and must determine to what extent the evidence for each key question—even evidence from screening RCTs or treatment RCTs—can be applied to the general primary care population. Frequently, studies are conducted in highly selected populations under special conditions. The USPSTF must consider differences between the general primary care population and the populations studied in RCTs and make judgments about the likelihood of observing the same effect in actual practice.

It is also important to note that one of the key questions in the analytic framework refers to the potential harms of the preventive service. The USPSTF considers the evidence about the benefits and harms of preventive services separately and equally. Data about harms are often obtained from observational studies because harms observed in RCTs may not be representative of those found in usual practice and because some harms are not completely measured and reported in RCTs.

Putting the body of evidence for all key questions together as a chain, the USPSTF assesses the certainty of net benefit of a preventive service by asking the 6 major questions listed above. The USPSTF would rate a body of convincing evidence about the benefits of a service that, for example, derives from several RCTs of screening in which the estimate of benefits can be generalized to the general primary care population as "high" certainty (see the "Rating Scheme for the Strength of the Recommendations" field). The USPSTF would rate a body of evidence that was not clearly applicable to general practice or has other defects in quality, research design, or consistency of studies as "moderate" certainty. Certainty is "low" when, for example, there are gaps in the evidence linking parts of the analytic framework, when evidence to determine the harms of treatment is unavailable, or when evidence about the benefits of treatment is insufficient. Table 4 in the methodology document listed below (see the "Availability of Companion Documents" field) summarizes the current terminology used by the USPSTF to describe the critical assessment of evidence at all 3 levels: individual studies, key questions, and overall certainty of net benefit of the preventive service.

Sawaya GF, Guirguis-Blake J, LeFevre M, Harris R, Petitti D; U.S. Preventive Services Task Force. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. *Ann Intern Med.* 2007;147(12):871-875. [5 references].

I Statements

For I statements, the USPSTF has a new plan to commission its Evidence-based Practice Centers to collect information in 4 domains pertinent to clinical decisions about prevention and to report this information routinely. This plan is described in the paper: Petitti DB et al. Update on the methods of the U.S. Preventive Services Task Force: insufficient evidence. *Ann Intern Med.* 2009;150:199-205. www.annals.org

The first domain is potential preventable burden of suffering from the condition. When evidence is insufficient, provision of an intervention designed to prevent a serious condition (such as dementia) might be viewed more favorably than provision of a service designed to prevent a condition that does not cause as much suffering (such as rash). The USPSTF recognized that "burden of suffering" is subjective and involves judgment. In clinical settings, it should be informed by patient values and concerns.

The second domain is potential harm of the intervention. When evidence is insufficient, an intervention with a large potential for harm (such as major surgery) might be viewed less favorably than an intervention with a small potential for harm (such as advice to watch less television). The USPSTF again acknowledges the subjective nature and the difficulty of assessing potential harms: for example, how bad is a "mild" stroke?

The third domain is cost—not just monetary cost, but opportunity cost, in particular the amount of time a provider spends to provide the service, the amount of time the patient spends to partake of it, and the benefits that might derive from alternative uses of the time or money for patients, clinicians, or systems. Consideration of clinician time is especially important for preventive services with only insufficient evidence because providing them could "crowd out" provision of preventive services with proven value, services for conditions that require immediate action, or services more desired by the patient. For example, a decision to routinely inspect the skin could take up the time available to discuss smoking cessation, or to address an acute problem or a minor injury that the patient considers important.

The fourth domain is current practice. This domain was chosen because it is important to clinicians for at least 2 reasons. Clinicians justifiably fear that not doing something that is done on a widespread basis in the community may lead to litigation. More important, addressing patient

expectations is a crucial part of the clinician–patient relationship in terms of building trust and developing a collaborative therapeutic relationship. The consequences of not providing a service that is neither widely available nor widely used are less serious than not providing a service accepted by the medical profession and thus expected by patients. Furthermore, ingrained care practices are difficult to change, and efforts should preferentially be directed to changing those practices for which the evidence to support change is compelling.

Although the reviewers did not explicitly recognize it when these domains were chosen, the domains all involve consideration of the potential consequences—for patients, clinicians, and systems—of providing or not providing a service. Others writing about medical decision making in the face of uncertainty have suggested that the consequences of action or inaction should play a prominent role in decisions.

Rating Scheme for the Strength of the Recommendations

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer/provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the "Clinical Considerations" section of USPSTF Recommendation Statement (see the "Major Recommendations" field). If this service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: <ul style="list-style-type: none"> • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice • Lack of coherence in the chain of evidence

Level of Certainty	Description
Low	<p>The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of:</p> <ul style="list-style-type: none"> • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice • A lack of information on important health outcomes <p>More information may allow an estimation of effects on health outcomes.</p>

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Comparison with Guidelines from Other Groups

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Peer Review. Before the U.S. Preventive Services Task Force (USPSTF) makes its final determinations about recommendations on a given preventive service, the Evidence-based Practice Center and the Agency for Healthcare Research and Quality send a draft evidence review to 4 to 6 external experts and to Federal agencies and professional and disease-based health organizations with interests in the topic. The experts are asked to examine the review critically for accuracy and completeness and to respond to a series of specific questions about the document. After assembling these external review comments and documenting the proposed response to key comments, the topic team presents this information to the USPSTF in memo form. In this way, the USPSTF can consider these external comments before it votes on its recommendations about the service. Draft recommendation statements are then circulated for comment among reviewers representing professional societies, voluntary organizations, and Federal agencies, as well as posted on the USPSTF Web site for public comment. These comments are discussed before the final recommendations are confirmed.

Response to Public Comment: A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 12 November to 9 December 2013. In response to these comments, the USPSTF added language emphasizing that the harms of β -carotene were found in persons at increased risk for lung cancer. The discussion of vitamin E was revised to clarify the consistency of evidence showing a lack of benefit. Additional language was added to the Research Needs and Gaps section to highlight other challenges in nutrient research. The Recommendations of Others section was enhanced with recommendations from additional organizations.

Comparison with Guidelines from Other Groups. Recommendations for vitamin and mineral supplementation from the following groups were discussed: the National Institutes of Health; the Academy of Nutrition and Dietetics (formerly the American Dietetic Association); the American Cancer Society; the American Institute for Cancer Research; the American Heart Association, and the American Academy of Family Physicians.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is not specifically stated for each recommendation.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Benefits of Vitamin Supplementation

The U.S. Preventive Services Task Force (USPSTF) found inadequate evidence on the benefits of supplementation with multivitamins to reduce the risk for cardiovascular disease or cancer. The USPSTF found inadequate evidence on the benefits of supplementation with individual vitamins or minerals or functional pairs in healthy populations without known nutritional deficiencies to reduce the risk for cardiovascular disease or cancer. The USPSTF found adequate evidence that supplementation with β -carotene or vitamin E in healthy populations without known nutritional deficiencies does not reduce the risk for cardiovascular disease or cancer.

Potential Harms

Harms of Vitamin Supplementation

The U.S. Preventive Services Task Force (USPSTF) found inadequate evidence on the harms of supplementation with multivitamins and most single vitamins or minerals or functional pairs. The USPSTF found adequate evidence that supplementation with β -carotene increases the risk for lung cancer in persons who are at increased risk for this condition. The USPSTF found adequate evidence that supplementation with vitamin E has few or no substantial harms.

Qualifying Statements

Qualifying Statements

- The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific clinical preventive care services for patients without related signs or symptoms.
- It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.
- The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.
- Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Implementation of the Guideline

Description of Implementation Strategy

The experiences of the first and second U.S. Preventive Services Task Force (USPSTF), as well as that of other evidence-based guideline efforts, have highlighted the importance of identifying effective ways to implement clinical recommendations. Practice guidelines are relatively weak tools for changing clinical practice when used in isolation. To effect change, guidelines must be coupled with strategies to improve their acceptance and feasibility. Such strategies include enlisting the support of local opinion leaders, using reminder systems for clinicians and patients, adopting standing orders, and audit and feedback of information to clinicians about their compliance with recommended practice.

In the case of preventive services guidelines, implementation needs to go beyond traditional dissemination and promotion efforts to recognize the added patient and clinician barriers that affect preventive care. These include clinicians' ambivalence about whether preventive medicine is part of their job, the psychological and practical challenges that patients face in changing behaviors, lack of access to health care or of insurance coverage for preventive services for some patients, competing pressures within the context of shorter office visits, and the lack of organized systems in most practices to ensure the delivery of recommended preventive care.

Dissemination strategies have changed dramatically in this age of electronic information. While recognizing the continuing value of journals and other print formats for dissemination, the USPSTF Task Force will make all its products available through its [Web site](#) . The combination of electronic access and extensive material in the public domain should make it easier for a broad audience of users to access USPSTF materials and adapt them for their local needs. Online access to USPSTF products also opens up new possibilities for the appearance of the annual, pocket-size Guide to Clinical Preventive Services.

To be successful, approaches for implementing prevention have to be tailored to the local level and deal with the specific barriers at a given site, typically requiring the redesign of systems of care. Such a systems approach to prevention has had notable success in established staff-model health maintenance organizations, by addressing organization of care, emphasizing a philosophy of prevention, and altering the training and incentives for clinicians. Staff-model plans also benefit from integrated information systems that can track the use of needed services and generate automatic reminders aimed at patients and clinicians, some of the most consistently successful interventions. Information systems remain a major challenge for individual clinicians' offices, however, as well as for looser affiliations of practices in network-model managed care and independent practice associations, where data on patient visits, referrals, and test results are not always centralized.

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Pocket Guide/Reference Cards

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

U.S. Preventive Services Task Force. Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2014 Apr 15;160(8):558-64. [26 references]
[PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2003 Jul 1 (revised 2014 Apr 15)

Guideline Developer(s)

U.S. Preventive Services Task Force - Independent Expert Panel

Guideline Developer Comment

The U.S. Preventive Services Task Force (USPSTF) is a federally-appointed panel of independent experts. Conclusions of the USPSTF do not necessarily reflect policy of the U.S. Department of Health and Human Services or its agencies.

Source(s) of Funding

The U.S. Preventive Services Task Force (USPSTF) is an independent, voluntary body. The U.S. Congress mandates that the Agency for Healthcare Research and Quality support the operations of the USPSTF.

Guideline Committee

U.S. Preventive Services Task Force

Composition of Group That Authored the Guideline

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**Members of the USPSTF at the time this recommendation was finalized. For a list of current Task Force members, go to <http://www.uspreventiveservicestaskforce.org/Page/Name/our-members> .*

Financial Disclosures/Conflicts of Interest

The U.S. Preventive Services Task Force (USPSTF) has an explicit policy concerning conflict of interest. All members disclose at each meeting if they have a significant financial, professional/business, or intellectual conflict for each topic being discussed. USPSTF members with conflicts may be recused from discussing or voting on recommendations about the topic in question.

Potential Conflicts of Interest: Dr. Moyer: *Support for travel to meetings for the study or other purposes*: Agency for Healthcare Research and Quality. Dr. Owens: *Support for travel to meetings for the study or other purposes*: U.S. Preventive Services Task Force. Dr. Pignone: *Grants/grants pending (money to institution)*: multiple federal awards, American Cancer Society, Informed Medical Decisions Foundation; *Royalties*: textbook chapters on lipids, prevention; *Travel/accommodations/meeting expenses unrelated to activities listed*: travel to meetings on aspirin prevention, Partnership for Prevention. Authors not named here have disclosed no conflicts of interest. Authors followed the policy regarding conflicts of interest described at www.uspreventiveservicestaskforce.org/methods.htm . Disclosures can also be

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Routine vitamin supplementation to prevent cancer and cardiovascular disease: recommendations and rationale. Ann Intern Med. 2003 Jul 1;139(1):51-5. [42 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the [Annals of Internal Medicine Web site](#) .

Availability of Companion Documents

The following are available:

Evidence Reviews:

- Fortmann SP, Burda BU, Senger CA, Lin JS, Beil TL, O'Connor E, Whitlock EP. Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer: a systematic evidence review for the U.S. Preventive Services Task Force. Evidence synthesis No. 108. AHRQ Publication No. 14-05199-EF-1. Rockville (MD): Agency for Healthcare Research and Quality; 2013 Nov. 186 p.
- Fortmann SP, Burda BU, Senger CA, Lin JS, Whitlock EP. Vitamin and mineral supplements in the primary prevention of cardiovascular disease and cancer: an updated systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013 Dec;159(12):824-834.

Electronic copies: Available from the [U.S. Preventive Services Task Force \(USPSTF\) Web site](#) .

Background Articles:

- Barton MB et al. How to read the new recommendation statement: methods update from the U.S. Preventive Services Task Force. Ann Intern Med 2007;147:123-127.
- Guirguis-Blake J et al. Current processes of the U.S. Preventive Services Task Force: refining evidence-based recommendation development. Ann Intern Med 2007;147:117-122.
- Sawaya GF et al. Update on the methods of the U.S. Preventive Services Task Force: estimating certainty and magnitude of net benefit. Ann Intern Med 2007;147:871-875.
- Petitti DB et al. Update on the methods of the U.S. Preventive Services Task Force: insufficient evidence. Ann Intern Med. 2009;150:199-205.

Electronic copies: Available from [USPSTF Web site](#) .

The following are also available:

- Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer. Clinical summary of U.S. Preventive Services Task Force recommendation. 2013 Nov. Electronic copies: Available from the [USPSTF Web site](#) .
- A continuing medical education (CME) activity is available from the [Annals of Internal Medicine Web site](#).
- The guide to clinical preventive services, 2012. Recommendations of the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ), 2012. 128 p. Electronic copies available from the [AHRQ Web site](#) . See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#) .

The [Electronic Preventive Services Selector \(ePSS\)](#) is an application designed to provide primary care clinicians and health care teams timely decision support regarding appropriate screening, counseling, and preventive services for their patients. It is based on the

current, evidence-based recommendations of the USPSTF and can be searched by specific patient characteristics, such as age, sex, and selected behavioral risk factors.

Patient Resources

The following are available:

- Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer. Understanding task force recommendations. U.S. Preventive Services Task Force. Consumer fact sheet. 2014 Feb. 5 p. Electronic copies: Available from the [U.S. Preventive Services Task Force \(USPSTF\) Web site](#) .
- Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer: recommendations from the U.S. Preventive Services Task Force. Summaries for patients. *Ann Intern Med*. 2014 Apr 15;160(8):I-24. Electronic copies: Available from the [Annals of Internal Medicine Web site](#) .
- Women: stay healthy at any age. 2014 update. Rockville (MD): Agency for Healthcare Research and Quality. AHRQ Pub. No. 14-IP007-A. 2014 Mar. 5 p. Electronic copies: Available in PDF in [English](#) and [Spanish](#) from the AHRQ Web site. See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#) .
- Men: stay healthy at any age. 2014 update. Rockville (MD): Agency for Healthcare Research and Quality. AHRQ Pub. No. 14-IP006-A. 2014 Mar. 5 p. Electronic copies: Available in PDF in [English](#) and [Spanish](#) from the AHRQ Web site. See the related QualityTool summary on the [Health Care Innovations Exchange Web site](#) .
- Women: stay healthy at 50+. 2014 update. Rockville (MD): Agency for Healthcare Research and Quality. AHRQ Pub. No. 14-IP002-A. 2014 Mar. 5 p. Electronic copies: Available in Portable Document Format (PDF) in [English](#) and [Spanish](#) from the AHRQ Web site.
- Men: stay healthy at 50+. 2014 update. Rockville (MD): Agency for Healthcare Research and Quality. AHRQ Pub. No. 14-IP009-A. 2014 Mar. 5 p. Electronic copies: Available in PDF in [English](#) and [Spanish](#) from the AHRQ Web site.

Print copies: Available in English and Spanish from the AHRQ Publications Clearinghouse. For more information, go to <http://www.ahrq.gov/research/publications/index.html> or call 1-800-358-9295  (U.S. only).

Myhealthfinder is a tool that provides personalized recommendations for clinical preventive services specific to the user's age, gender, and pregnancy status. It features evidence-based recommendations from the USPSTF and is available at www.healthfinder.gov .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI on June 24, 2003. This summary was verified by the developer on June 26, 2003. This summary was updated by ECRI Institute on May 19, 2014. The updated information was verified by the guideline developer on June 5, 2014.

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